

PRELIMINARY REMARKS

Claims 27 to 49 as set forth in Appendix I of this paper are herewith presented for further prosecution. Relative to the previous version of claims, Claims 1 to 10, 12 to 14 and 16 to 24 have been canceled, and Claims 27 to 49 have been added, as indicated in the listing of the claims. More specifically:

Claims 9 and 10 have been rewritten as new Claims 27 and 28. In rewriting Claim 9, the wording has been revised to bring out that at least one aromatic C-H group of an N- or S-heterocyclic mono- or polynuclear aromatic moiety of a compound be oxidized.²⁾ Additionally, the wording has been revised to bring out that the mutation of SEQ ID NO:2 consists of one or more of the recited functional mutations.

A new Claim 29 has been added, which corresponds to previous Claim 2 with the difference that the additional new claim depends upon Claim 27.

Claims 12, 17 and 18 have been rewritten as new Claims 30, 31 and 32, respectively. In rewriting Claims 17 and 18, the wording has been revised to remove the phrase >>as exogenous substrate<<.

Claims 19 to 23 which stood withdrawn from consideration have been rewritten as new Claims 33 to 37. In rewriting Claim 22, the wording has been revised to bring out that the mutation of SEQ ID NO:2 consists of one or more of the recited functional mutations.

Claims 1 to 8 which stood withdrawn from consideration have been rewritten as new Claims 38 to 45. In rewriting Claim 1, the wording has been revised to bring out that the mutation of SEQ ID NO:2 consists of one or more of the recited functional mutations.

Claims 13, 14, 16 and 24 which stood withdrawn from consideration have been rewritten as new Claims 46 to 49. In rewriting Claim 13, the wording has been revised to bring out that the mutation of SEQ ID NO:2 consists of one or more of the recited functional mutations.

No new matter has been added by the revisions of the claims. Entry and favorable consideration is respectfully solicited.

Claims 17 and 18 were rejected under 35 U.S.C. §112, ¶2, as allegedly being rendered indefinite by the phrase >>as exogenous substrate<<. New Claims 31 and 32 which replace Claims 17

2) Cf., e.g., page 2, indicated lines 35 to 40, in conjunction with page 5, indicated lines 11 to 41, and page 11, indicated line 42, to page 13, indicated line 40, of the application.

and 18 do not recite the respective phrase, and the rejection therefore does not apply to the new claims. It is respectfully requested that the rejection be withdrawn. Favorable action is solicited.

Claims 9, 10, 12 and 17 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by the teaching of *Wong et al.* (GB 2 294 692),³⁾ and under 35 U.S.C. §102(b) as allegedly being anticipated by the teaching of *Flitsch et al.* (US 6,100,074).

Anticipation under Section 102 can be found only if a reference shows exactly what is claimed, i.e., all material elements of the invention as claimed must be found in one prior art source,⁴⁾ the elements must be shown in the reference in as much detail as is contained in the claim,⁵⁾ and the elements must be shown in the reference in the part-to-part relationship which is set forth in the claim.⁶⁾

Neither one of the teachings of *Wong et al.* and *Flitsch et al.* shows exactly what is claimed in new Claims 27, 28, 30 and 31 which replace Claims 9, 10, 12 and 17, and the rejection therefore does not apply to the new claims.

Claim 27 specifies that at least one aromatic C-H group of an N- or S-heterocyclic mono- or polynuclear aromatic moiety of a compound be oxidized in the claimed process and the respective requirement is incorporated by reference in Claims 28 to 31.

The teaching of *Wong et al.* pertains to a mutant of the monooxygenase cytochrome P-450_{cam} in which at least a tyrosine residue at position 96 and/or a cysteine residue at position 334 is replaced by the residue of any other amino acid.⁷⁾ The mutant catalyzes the oxidation of polycyclic aromatic hydrocarbons, linear or branched alkanes, diphenyl and biphenyl compounds including halogenated variants of such compounds and halogenated hydrocarbons.⁸⁾ Hydrocarbons consist of carbon and hydrogen.⁹⁾ The referenced substrate groups, therefore, do not encompass *N*- or *S*-heterocyclic mono- or polynuclear aromatic moieties.

3) As an aside it is noted that the disclosure of a British reference is not applicable as prior art under the provisions of Section 102(e).

4) Cf. *In re Marshall*, 577 F.2d 301, 198 USPQ 344 (CCPA 1978); *In re Kalm*, 378 F.2d 959, 154 USPQ 10 (CCPA 1967).

5) Cf. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 9 USPQ2d 1913 (Fed. Cir. 1989).

6) Cf. *Lindemann Maschinenfabrik v. American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984).

7) I.e. Abstract of GB 2 294 692.

8) Page 4, paras. 2 and 3, of GB 2294 682.

9) Hawley's Condensed Chemical Dictionary, 13th Ed., John Wiley & Sons, Inc., 1997; ISBN 0-471-29205-2; page 587, copy enclosed.

Compounds which comprise a heterocyclic aromatic moiety are delineated in Scheme 1, on page 14 of *Wong et al.* However, the reference makes clear that the depicted benzoxazole group functions as a protection group rather than a substrate group: “*Examples of monofunctionalised hydrocarbons are cyclohexyl, cyclopentyl and alkyl derivatives (Scheme 1). The oxidation products of these compounds are valuable starting materials for organic synthesis, particularly when produced in a homochiral form. A range of aromatic protecting groups are envisaged, e.g. benzyl or naphthyl ether and benzoyl or naphthoyl esters and amids (Scheme 1). Of interest are also benzoxazole groups as carboxyl protecting groups and N-benzyl oxazolidine groups as aldehyde protecting groups. Both can be easily cleaved after the enzymatic oxidation and have previously been described in the literature for the microbial oxidations of aldehydes and acids.*”¹⁰⁾

Similarly, the teaching of *Flitsch et al.* pertains to a mutant of the monooxygenase cytochrome P-450_{cam} in which at least a tyrosine residue at position 96 and/or a cysteine residue at position 334 is replaced by the residue of any other amino acid¹¹⁾ which catalyzes the oxidation of polycyclic aromatic hydrocarbons, linear or branched alkanes, diphenyl and biphenyl compounds including halogenated variants of such compounds and halogenated hydrocarbons.¹²⁾ Like *Wong et al.*, *Flitsch et al.* mention benzoxazole merely as a carboxyl protecting group.¹³⁾

Both *Wong et al.* and *Flitsch et al.* point out: “*Thus the protecting group serves two purposes: firstly it makes the substrate more hydrophobic and hence increases binding to the hydrophobic enzyme pocket; secondly it holds the substrate in place at the active site. Thus, with the correct aromatic protection group, both regio-and stereo-selective hydroxylation of the substrate may be achieved.*”¹⁴⁾ Accordingly, the substrate group, i.e., the optionally halogenated hydrocarbon residue of the compound, and not the protecting group, is being oxidized in accordance with the teaching of the references.

Neither *Wong et al.* nor *Flitsch et al.* describe, or even suggest, an oxidation by which “*at least one aromatic C-H group*” of an N- or S-heterocyclic mono- or polynuclear aromatic moiety of a compound is oxidized as is required in accordance with Claims 27, 28, 30 and 31. The rejections under Section 102, therefore, do not apply to the new claims, and it is respectfully requested that the rejections be withdrawn. Favorable action is solicited.

10) Page 7, last para., of *GB 2 294 692*.

11) I.e. Abstract of *US 6,100,074*.

12) Col. 2, indicated lines 28 to 48, of *US 6,100,074*.

13) Scheme 1 in cols. 5 and 6, and col. 3, indicated lines 49 to 61, of *US 6,100,074*.

14) Page 7, para. 2, of *GB 2294 692* and col. 3, indicated lines 40 to 48, of *US 6,100,074*.

Claims 9, 10, 12, 17 and 18 were rejected under 35 U.S.C. §112, ¶1, for allegedly failing to comply with the written description requirement.

More specifically the Office action asserted, in part, “the claims are not limited to a variant of SEQ ID NO:2 comprising of mutations at the recited regions.” New Claims 27, 28 and 30 to 32 which replace Claims 9, 10, 12, 17 and 18 inter alia set forth that the mutation consists of at least one functional mutation in at least one of the amino acid sequence regions 172–224, 39–43, 48–52, 67–70, 330–335, 352–356, 73–82 and 86–88 of SEQ ID NO:2. The respective argument, therefore, does not apply to the new claims presented herewith.

The Office action also argued that the written description requirement was not met because “the specification only describes one representative species ...” To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.¹⁵⁾ An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.¹⁶⁾ Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was “ready for patenting” such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.¹⁷⁾ Accordingly, “(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.”¹⁸⁾

Applicants have described the mutant monooxygenases as well as the substrate compounds not merely by including description of an actual reduction to practice but also, inter alia, by distin-

15) MPEP §2163(I), Rev. 6, Sept. 2007, citing *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

16) MPEP §2163(I), Rev. 6, Sept. 2007, citing *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

17) MPEP §2163(I), Rev. 6, Sept. 2007, citing *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

18) *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006)

guishing identifying characteristics.¹⁹⁾ One having ordinary skill in the pertinent art will readily recognize in applicants' disclosure a description of the subject matter defined by the claims.²⁰⁾ The rejection therefore does not apply to the claims presented herewith, and it is respectfully requested that the rejection be withdrawn. Favorable action is solicited.

Claims 9, 10, 12, 17 and 18 were rejected under 35 U.S.C. §112, ¶1, for allegedly failing to comply with the enablement requirement.

More specifically the Office action again asserted that the mutations of SEQ ID NO:2 were not limited to the recited substitution positions and argued that guidance with regard to which specific amino acids can be modified was lacking.

New Claims 27, 28 and 30 to 32 which replace Claims 9, 10, 12, 17 and 18 inter alia set forth that the mutation consist of at least one functional mutation in at least one of the amino acid sequence regions 172–224, 39–43, 48–52, 67–70, 330–335, 352–356, 73–82 and 86–88 of SEQ ID NO:2. The respective argument, therefore, does not apply to the new claims presented herewith. It is therefore respectfully requested that the rejection be withdrawn. Favorable action is solicited.

19) E.g., page 2, indicated lines 22 to 44, page 3, indicated lines 15 to 26, and page 5, indicated lines 11 to 41, of the application.

20) Cf. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).